A Boundary Integral Formulation for Nonlocal Electrostatics

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Abstract In the field of protein binding, it is important to gain some knowledge about the electric field surrounding the concerning biomolecules. Most of the interesting action takes place inside cells where the medium is similar to water, which is a nonlocal medium. To handle this nonlocal behavior caused by a network of hydrogen bonds, we formulate an interface problem in terms of a system of coupled partial differential equations involving the Laplace and the Yukawa operator. Furthermore, we deduce for the system a fundamental solution and an associated representation formula. We finally derive a boundary integral formulation to determine the complete Dirichlet and Neumann data.

1 Modelling Nonlocal Electrostatics for Biomolecules in Water

The model given below is a modification of the model as presented in [1, 2]. Before going into detail, we first introduce some notations. Let $\Omega^i \subset \mathbb{R}^3$ be a bounded domain where the molecule is located. Let $\Omega^e = \mathbb{R}^3 \setminus \overline{\Omega}^i$ denote the unbounded domain exterior to Ω^i which is filled with water. $\Gamma = \mathbb{R}^3 \setminus (\Omega^i \cup \Omega^e)$ is the interface between the molecule and water. For $x \in \Gamma$ we define the normal vector $\mathbf{n}(x)$ as the unit vector pointing from Ω^i into Ω^e. The interior and exterior trace operators are denoted by γ_0^{int} and γ_0^{ext}, respectively.

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The starting point for our considerations are the Maxwell equations of electrostatics which describe the behavior of the electric field $\mathbf{E}$ and of the displacement field $\mathbf{D}$ by

$$\operatorname{curl} \mathbf{E}(x) = 0, \qquad x \in \Omega^i \cup \Omega^e, \tag{1}$$

$$\operatorname{div} \mathbf{D}(x) = \rho(x), \quad x \in \Omega^i \cup \Omega^e. \tag{2}$$

The charge distribution is modelled as a sum of partial charges located inside Ω^i,

$$\rho(x) = \sum_{j=1}^{N_c} q_j \delta(x - x_j), \tag{3}$$

where δ denotes the Dirac Delta distribution. Furthermore, it is known that – in absence of surface charges – the tangential component of the electric field and the normal component of the displacement field are continuous through the interface,

$$(\gamma_0^{int}\mathbf{E}(x) - \gamma_0^{ext}\mathbf{E}(x)) \times \mathbf{n}(x) = 0, \qquad x \in \Gamma, \tag{4}$$

$$(\gamma_0^{int}\mathbf{D}(x) - \gamma_0^{ext}\mathbf{D}(x), \mathbf{n}(x)) = 0, \qquad x \in \Gamma. \tag{5}$$

One of the main steps in the modelling is the description of the relation between $\mathbf{E}$ and $\mathbf{D}$. Inside the molecule we assume a local relationship, and therefore,

$$\mathbf{D}(x) = \varepsilon_0 \varepsilon_{\Omega^i} \mathbf{E}(x), \quad x \in \Omega^i, \tag{6}$$

where ε_0 is the permittivity of vacuum, and ε_{Ω^i} is constant inside the molecule. The description in Ω^e is more complicated due to the nonlocal effects of water. There are two different facts that influence the relation between the two fields in Ω^e. Each water molecule can be seen as a dipole and thus would normally align itself with the field and all together would cause a relatively strong shielding effect. On the other side, water molecules build a network of hydrogen bonds. This network has energetic advantages and is strongly dependent on the angle of the water molecules towards each other. The strength of the electric field determines if the water keeps the bonds or aligns with the field. That is the reason why the electric field in the neighbourhood of a point x is important for the displacement field in the point in contrast to the local relationship where only the electric field in the point has to be taken into account. The nonlocal relationship is taken as

$$\mathbf{D}(x) = \varepsilon_0 \left(\varepsilon_\infty \mathbf{E}(x) + \eta^2 \int_{\Omega^e} \frac{e^{-\kappa|x-y|}}{4\pi|x-y|} \mathbf{E}(y)\, dy \right), \quad x \in \Omega^e, \tag{7}$$

where

$$\eta^2 = (\varepsilon_{\Omega^e} - \varepsilon_\infty)\kappa^2, \quad \kappa = \frac{1}{\lambda},$$

λ is the correlation length, and ε_∞ and ε_{Ω^e} are constants describing the dielectricity of the material. The scaling of the system is done with respect to the typical length of an hydrogen bond.

To transfer this system of partial-integro-differential equations into a system of partial differential equations, we make use of a scalar potential for $\mathbf{E}$,

$$\mathbf{E}(x) = -\nabla\varphi(x), \quad x \in \Omega^i \cup \Omega^e. \tag{8}$$

Then, the electric field $\mathbf{E}$ is curl-free and with respect to φ, the material relations can be written as

$$\mathbf{D}(x) = -\varepsilon_{\Omega^i}\nabla\varphi(x), \quad x \in \Omega^i, \tag{9}$$

$$\mathbf{D}(x) = -\varepsilon_\infty\nabla\varphi(x) - \eta^2 \int_{\Omega^e} \frac{e^{-\kappa|x-y|}}{4\pi|x-y|}\nabla\varphi(y)\,dy, \quad x \in \Omega^e. \tag{10}$$

Note that the constant ε_0 has been eliminated during the process of scaling. Applying the divergence to (9) and to (10), it follows by the use of (2) and (8) that

$$-\varepsilon_{\Omega^i}\Delta\varphi(x) = \rho(x), \quad x \in \Omega^i, \tag{11}$$

$$-\varepsilon_\infty\Delta\varphi(x) - \eta^2 \mathrm{div} \int_{\Omega^e} \frac{e^{-\kappa|x-y|}}{4\pi|x-y|}\nabla\varphi(y)\,dy = 0, \quad x \in \Omega^e. \tag{12}$$

In addition, the transmission condition (4) for the electric field takes the form

$$\gamma_0^{int}\varphi(x) = \gamma_0^{ext}\varphi(x), \quad x \in \Gamma. \tag{13}$$

In order to eliminate the volume integral in (12) we introduce an additional unknown function which we denote by $\mathbf{P}$. It is defined as

$$\mathbf{P}(x) = -\eta \int_{\Omega^e} \frac{e^{-\kappa|x-y|}}{4\pi|x-y|}\nabla\varphi(y)\,dy, \quad x \in \Omega^i \cup \Omega^e. \tag{14}$$

$\mathbf{P}$ describes the polarisation in Ω^e, but has no physical meaning in Ω^i. With this, equation (12) reads

$$-\varepsilon_\infty\Delta\varphi(x) + \eta\,\mathrm{div}\,\mathbf{P}(x) = 0, \quad x \in \Omega^e, \tag{15}$$

and the transmission condition (5) for the displacement field becomes

$$\varepsilon_{\Omega^i}\gamma_1^{int}\varphi(x) = \varepsilon_\infty\gamma_1^{ext}\varphi(x) - \eta\,(\gamma_0^{ext}\mathbf{P}(x), \mathbf{n}(x)), \quad x \in \Gamma, \tag{16}$$

where $\gamma_1^{int/ext}$ denotes the interior and exterior conormal derivative, respectively. To find a second relation between φ and $\mathbf{P}$, we use the Yukawa operator $\mathscr{L}_\kappa = \Delta - \kappa^2$, and the fact that the convolution kernel under the integral is its fundamental solution. Thus, we obtain

$$-\mathscr{L}_\kappa \mathbf{P}(x) + \eta \nabla \varphi(x) = 0\,, \quad x \in \Omega^e, \tag{17}$$

$$-\mathscr{L}_\kappa \mathbf{P}(x) = 0\,, \quad x \in \Omega^i. \tag{18}$$

Transmission conditions for the field $\mathbf{P}$ can be deduced from (14) as

$$\gamma_0^{ext}\mathbf{P}(x) = \gamma_0^{int}\mathbf{P}(x)\,, \quad \gamma_1^{ext}\mathbf{P}(x) = \gamma_1^{int}\mathbf{P}(x)\,, \quad x \in \Gamma. \tag{19}$$

To complete the system, we include radiation conditions for φ and $\mathbf{P}$, where the one for $\mathbf{P}$ can be deduced from the one for φ,

$$\varphi(x) \sim \frac{1}{|x|}\,, \quad |\mathbf{P}(x)| \sim \frac{1}{|x|^2} \quad \text{as } |x| \to \infty. \tag{20}$$

The resulting system composed by (11), (13), (15), (16), (17), (18), (19), and (20), is a system of purely partial differential equations that is equivalent to the mixed partial-integro-differential system we started from.

2 Analytical and Fundamental Solution

For the special case of only one charge with strength q, located in the origin of a sphere with radius a, we can transfer all differential operators into spherical coordinates. Then we are able to find an analytical solution, namely

$$\varphi^{int}(x) = \frac{q}{4\pi\varepsilon_{\Omega_i}|x|} + \frac{q}{4\pi a}\left(\frac{1}{\varepsilon_{\Omega_e}} - \frac{1}{\varepsilon_{\Omega_i}} + B\frac{e^{-\kappa' a}}{4\pi a}\right),$$

$$\varphi^{ext}(x) = \frac{q}{4\pi\varepsilon_{\Omega_e}}\left(\frac{1}{|x|} + B\frac{e^{-\kappa'|x|}}{|x|}\right),$$

$$\mathbf{P}^{int}(x) = C\frac{q}{4\pi\varepsilon_{\Omega^e}}\frac{(e^{\kappa|x|}(\kappa|x|-1) + e^{-\kappa|x|}(\kappa|x|-1)}{|x|^3}x,$$

$$\mathbf{P}^{ext}(x) = \frac{q}{4\pi\varepsilon_{\Omega_e}|x|^3}\left(\frac{1}{\kappa^2} + B\frac{e^{-\kappa'|x|}(1+\kappa'|x|)}{\kappa^2 - \kappa'^2}\right)x,$$

where

$$\kappa'^2 = \kappa^2 + \frac{\eta^2}{\varepsilon_\infty}\,,$$

and the constants B and C are given by

$$B = \frac{\eta(\kappa'^2 - \kappa^2)(e^{\kappa a} - e^{-\kappa a})e^{\kappa' a}}{e^{\kappa a}(\kappa^2(\kappa' a + 1) + \kappa'^2(\kappa a - 1)) + e^{-\kappa a}(\kappa'^2(\kappa a + 1) - \kappa^2(\kappa' a + 1))}\,,$$

$$C = \frac{\eta\kappa'^2}{\kappa^2}\frac{1}{e^{\kappa a}(\kappa^2(\kappa' a + 1) + \kappa'^2(\kappa a - 1)) + e^{-\kappa a}(\kappa'^2(\kappa a + 1) - \kappa^2(\kappa' a + 1))}\,.$$

This example also shows that the model contains the local case. In the local case we have $\lambda \to 0$ which induces $\kappa \to \infty$, and also $\kappa' \to \infty$. For $\kappa' \to 0$ the exponential term in φ^{ext} disappears, and we end up with the solution of the local system, namely,

$$\varphi^{ext}(x) = \frac{q}{4\pi\varepsilon_{\Omega_e}|x|}, \quad \lambda \to 0 .$$

Furthermore, the analytical solution can be used to control future numerical results with respect to their reliability.

In general, the system derived cannot be solved analytically, instead we have to use some numerical approach. Since the domain Ω^i may have a very complicated boundary Γ which is usually given already in a discretized form (see Fig. 1 for the Solvent Excluded Surface of the neurotransmitter Acetylcholinesterase) the use of a boundary integral equation approach seems to be favourable. Moreover, the exterior domain Ω^e is unbound, therefore a boundary element method seems to be more advantageous than a finite element method.

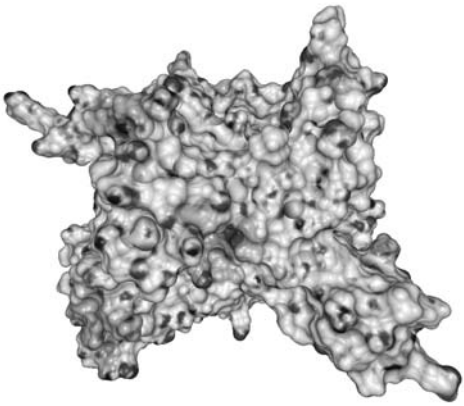

Fig. 1 Solvent excluded surface of Acetylcholinesterase, Source: BALLView [4]

To obtain a boundary integral formulation we first have to consider the interior and the exterior problem separately.

In the interior domain Ω^i we have to deal with the Laplace and with the Yukawa operator, both are well known, for their representation formulae and potentials see e.g., [3, 5, 6]. Thus we will skip this part here and make use of their results later.

To handle the partial differential equation in the exterior domain Ω^e we define the operator

$$\mathscr{A}^{ext} = \begin{pmatrix} -\varepsilon_{\Omega^e}\Delta & \eta\nabla^T \\ \eta\nabla & -\mathscr{L}_\kappa I_3 \end{pmatrix} \tag{21}$$

which turns out to be elliptic. Because of the first order derivatives involved, the operator $\mathscr{A}^{ext}$ is not self-adjoint and, thus, we need to compute the fundamental

solution of the adjoint operator to obtain a representation formula for the exterior problem. Since the coefficients of $\mathscr{A}^{ext}$ are constant, we are able to find the fundamental solution by using the Fourier transform and obtain

$$\mathscr{U}^*_{ext}(x,y) = \begin{pmatrix} f_1 & (x-y)^T f_2 \\ (x-y) f_2 & f_3 I_3 + (x-y)(x-y)^T f_4 \end{pmatrix}, \tag{22}$$

where

$$\begin{aligned}
f_1 &= \frac{(\kappa'^2 - \kappa^2) e^{-\kappa'|x-y|} + \kappa^2}{4\pi\varepsilon_\infty \kappa'^2 |x-y|}, \\
f_2 &= -\frac{\eta}{4\pi\varepsilon_\infty \kappa'^2} \frac{e^{-\kappa'|x-y|}(\kappa'|x-y|+1) - 1}{|x-y|^3}, \\
f_3 &= \frac{e^{-\kappa|x-y|}}{4\pi|x-y|} + \frac{e^{-\kappa|x-y|}(\kappa|x-y|+1) - 1}{4\pi\kappa^2|x-y|^3} - \frac{e^{-\kappa'|x-y|}(\kappa'|x-y|+1) - 1}{4\pi\kappa'^2|x-y|^3}, \\
f_4 &= \frac{e^{-\kappa'|x-y|}(\kappa'^2|x-y|^2 + 3\kappa'|x-y| + 3) - 3}{4\pi\kappa'^2|x-y|^5} - \\
&\quad - \frac{e^{-\kappa|x-y|}(\kappa^2|x-y|^2 + 3\kappa|x-y| + 3) - 3}{4\pi\kappa^2|x-y|^5}.
\end{aligned}$$

A closer look at the fundamental solution clearly indicates that the only singularities are included in f_1 and in the first part of f_3. Both are first order singularities.

3 Representation Formula and Boundary Integral Formulation

The representation formula is obtained in the usual way by multiplying the partial differential equation with an appropriate test function and integrating over the exterior domain. Afterwards we apply the adjoint operator to the test function, multiply with the solution of the original problem and once again integrate by parts. We end up with the following representation formula for $x \in \Omega^e$

$$\begin{pmatrix} \varphi \\ \mathbf{P} \end{pmatrix}(x) = -\int_\Gamma \gamma_0^{ext} \mathscr{U}^*_{ext}(x,y) \begin{pmatrix} \varepsilon_\infty \gamma_1^{ext} \varphi - \eta(\gamma_0^{ext}\mathbf{P}, \mathbf{n}) \\ \gamma_1^{ext}\mathbf{P} \end{pmatrix} ds_y + \int_\Gamma W(x,y) \begin{pmatrix} \gamma_0^{ext}\varphi \\ \gamma_0^{ext}\mathbf{P} \end{pmatrix} ds_y,$$

where W is given as

$$\begin{aligned}
W_{11} &= \varepsilon_\infty \gamma_{1,y}^{ext} f_1 + \eta(\gamma_0^{ext}(x-y) f_2, \mathbf{n}(y)), \\
W_{12} &= \gamma_{1,y}^{ext}((x-y)_1 f_2), \\
W_{13} &= \gamma_{1,y}^{ext}((x-y)_2 f_2), \\
W_{14} &= \gamma_{1,y}^{ext}((x-y)_3 f_2), \\
W_{21} &= \varepsilon_\infty \gamma_{1,y}^{ext}(x-y)_1 f_2 + \eta \gamma_0^{ext}(f_3 \mathbf{e}_1 + (x-y)_1 (x-y) f_4), \mathbf{n}(y)),
\end{aligned}$$

$$
\begin{aligned}
W_{22} &= \gamma_{1,y}^{ext}(f_3 + (x-y)_1^2 f_4),\\
W_{23} &= \gamma_{1,y}^{ext}((x-y)_1(x-y)_2 f_4) = W_{32},\\
W_{24} &= \gamma_{1,y}^{ext}((x-y)_1(x-y)_3 f_4) = W_{42},\\
W_{31} &= \varepsilon_\infty \gamma_{1,y}^{ext}(x-y)_2 f_2 + \eta\,\gamma_0^{ext}(f_3\mathbf{e}_2 + (x-y)_2(x-y)f_4), \mathbf{n}(y)),\\
W_{33} &= \gamma_{1,y}^{ext}(f_3 + (x-y)_2^2 f_4),\\
W_{34} &= \gamma_{1,y}^{ext}((x-y)_2(x-y)_3 f_4) = W_{43},\\
W_{41} &= \varepsilon_\infty \gamma_{1,y}^{ext}(x-y)_3 f_2 + \eta\,\gamma_0^{ext}(f_3\mathbf{e}_3 + (x-y)_3(x-y)f_4), \mathbf{n}(y)),\\
W_{44} &= \gamma_{1,y}^{ext}(f_3 + (x-y)_3^2 f_4).
\end{aligned}
$$

To come up with a boundary integral equation, we follow the direct BEM approach and apply the exterior trace operator γ_0^{ext} to the above representation formula. For the calculation of the matrix entries in the BEM method, we can separate the integrals in parts that are those of the Laplace operator and some additional parts that can be calculated by numerical integration. Mapping properties can be transferred from the ones for the Laplace operator. We end up with the following boundary integral equation

$$
V_{nl}\begin{pmatrix} \gamma_1^{ext}\varphi - \eta(\gamma_0^{ext}\mathbf{P},\mathbf{n}) \\ \gamma_1^{ext}\mathbf{P} \end{pmatrix} = -\frac{1}{2}\gamma_0^{ext}\begin{pmatrix}\varphi\\ \mathbf{P}\end{pmatrix} + K_{nl}\gamma_0^{ext}\begin{pmatrix}\varphi\\ \mathbf{P}\end{pmatrix}, \tag{23}
$$

where

$$
(V_{nl}u)(x) = \gamma_{0,x}^{ext}\int_\Gamma \mathscr{U}_{ext}^*(x,y)u(y)\,ds_y, \tag{24}
$$

$$
(K_{nl}w)(x) = \lim_{\varepsilon\to 0}\int\limits_{y\in\Gamma:|x-y|\geq\varepsilon} W(x,y)w(y)\,ds_y \tag{25}
$$

are the associated single and double layer potential, respectively. In the interior domain Ω^i we obtain by using the particular solution

$$
\mathbf{u}_p(x) = \left(\sum_{j=1}^{N_c}\frac{q_j}{4\pi|x-x_j|}, 0, 0, 0\right)^\top
$$

the boundary integral equation

$$
V_{loc}\gamma_1^{int}\begin{pmatrix}\varphi\\ \mathbf{P}\end{pmatrix} = \frac{1}{2}\gamma_0^{int}\begin{pmatrix}\varphi\\ \mathbf{P}\end{pmatrix} + K_{loc}\gamma_0^{int}\begin{pmatrix}\varphi\\ \mathbf{P}\end{pmatrix} - \gamma_0^{int}\mathbf{u}_p \tag{26}
$$

where

$$
V_{loc} = \begin{pmatrix} V_0 & 0 & 0 & 0\\ 0 & V_\kappa & 0 & 0\\ 0 & 0 & V_\kappa & 0\\ 0 & 0 & 0 & V_\kappa\end{pmatrix} \text{ and } K_{loc} = \begin{pmatrix} K_0 & 0 & 0 & 0\\ 0 & K_\kappa & 0 & 0\\ 0 & 0 & K_\kappa & 0\\ 0 & 0 & 0 & K_\kappa\end{pmatrix}.
$$

V_0 and V_κ denote the single layer potentials of the Laplace and of the Yukawa operator, while K_0 and K_κ denote their double layer potentials. Using the interface conditions (13), (16), and (19), we finally obtain the desired boundary integral equation

$$\left(\begin{pmatrix}\varepsilon_{\Omega^i} & \\ & I_3\end{pmatrix} V_{loc}^{-1}\left(\frac{1}{2}I+K_{loc}\right)-V_{nl}^{-1}\left(-\frac{1}{2}I+K_{nl}\right)\right)\gamma_0\mathbf{u}=\begin{pmatrix}\varepsilon_{\Omega^i} & \\ & I_3\end{pmatrix} V_{loc}^{-1}\gamma_0\mathbf{u}_p\,, \quad (27)$$

where

$$\gamma_0\mathbf{u}=\left(\gamma_0^{int}\varphi,\gamma_0^{int}\mathbf{P}\right)^\top=\left(\gamma_0^{ext}\varphi,\gamma_0^{ext}\mathbf{P}\right)^\top.$$

Note that the Laplace and Yukawa single layer potentials are elliptic and therefore invertible, and the same holds true for the nonlocal exterior operator. Solving the boundary integral equation (27) leads to the knowledge of the Dirichlet data $\gamma_0\mathbf{u}$ on Γ. When knowing this function, we can calculate the interior Neumann data by solving an associated Dirichlet boundary value problem. The complete Cauchy data of the interior problem then provides the possibility to calculate the exterior Neumann data by using the corresponding transmission condition. In this way, we receive the complete set of Cauchy data for both problems. By the use of the representation formulae in Ω^i and Ω^e, we can evaluate the solution everywhere in $\mathbb{R}^3$.

4 Outlook

Based on the boundary integral equation (27) we are going to solve the problem by using modern boundary element techniques. A good approximation strategy for the matrices based on fast BEM (cf. [5]) has to be chosen to obtain reasonable results in a realistic time. Another major task for future work is the numerical analysis of the approximation scheme.

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